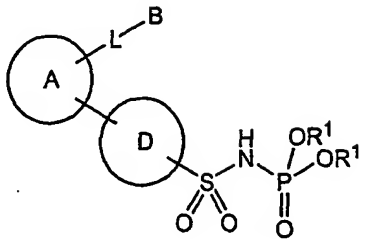
CLAIMS

1.- A compound of general formula I:



I

wherein:

each R^1 independently represents hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, phenyl, heteroaryl or phenylC_{1-3} alkyl, where all phenyl and heteroaryl rings can be optionally substituted with one or more halogen, C_{1-4} alkyl or C_{1-4} alkoxy groups, or both substituents R^1 may be taken together to form a saturated or partially unsaturated 5- or 6-membered ring, which can be optionally fused to a benzene ring;

A represents an unsaturated or partially unsaturated 5- or 6-membered ring which can optionally contain from 1 to 3 heteroatoms selected from N, O and S, where the substituents L and D are placed on adjacent atoms of ring A, and where additionally A can be optionally substituted with one or more substituents R^2;

L represents a single bond, -O-, -S- or -NR^3-;

B represents C_{1-6} alkyl or a ring selected from phenyl, heteroaryl and C_{3-7} cycloalkyl, where all said rings can be optionally substituted with one or more substituents R^4;

D represents phenyl or pyridine, which can be both optionally substituted with one or more halogens;

the groups A and -$SO_2NHP(O)(OR^1)_2$ are placed on ring D in *para* position with respect to one another;

each R^2 independently represents halogen, cyano, nitro, carboxy, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} haloalkyl, hydroxy, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, amino, C_{1-4} alkylamino, C_{1-4} dialkylamino, formyl, C_{1-4} alkylcarbonyl, C_{1-4} alkoxycarbonyl, C_{1-4} haloalkoxycarbonyl, C_{1-4} alkoxyC_{1-3} alkyl,

C_{1-4} alkylcarbonyloxyC_{1-3} alkyl, C_{3-7} cycloalkylC_{1-4} alkoxyC_{1-3} alkyl or C_{3-7} cycloalkoxyC_{1-3} alkyl, or two substituents R^2 on the same carbon atom can be taken together to form an oxo group;

R^3 represents hydrogen or C_{1-4} alkyl;

each R^4 independently represents halogen, cyano, nitro, carboxy, C_{1-4} alkyl, C_{1-4} haloalkyl, hydroxy, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, amino, C_{1-4} alkylamino, C_{1-4} dialkylamino, formyl, C_{1-4} alkylcarbonyl, C_{1-4} alkoxycarbonyl or C_{1-4} haloalkoxycarbonyl, or two substituents R^4 on the same carbon atom can be taken together to form an oxo group, and additionally one of the substituents R^4 can represent a saturated, unsaturated or partially unsaturated 5- or 6-membered ring which can optionally contain from 1 to 3 heteroatoms selected from N, O and S and which can be optionally substituted with one or more substituents R^5;

each R^5 independently represents halogen, hydroxy, nitro, cyano, amino, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy or C_{1-4} alkylcarbonyl, or two substituents R^5 on the same carbon atom can be taken together to form an oxo group; and

heteroaryl in the above definitions represents pyridine, pyrazine, pyrimidine or pyridazine;

and the salts and solvates thereof.

2.- A compound according to claim 1 wherein A represents imidazole, pyrazole, isoxazole, oxazole, thiazole, 2,5-dihydrofuran, thiophene, pyridine, 4*H*-pyran, cyclopentene, 2,3-dihydrooxazole or 4,5-dihydropyrazole which can be optionally substituted with one to four substituents R^2.

3.- A compound according to claim 2 wherein A represents imidazole, pyrazole, isoxazole, oxazole, 2,5-dihydrofuran or 4*H*-pyran which can be optionally substituted with one to four substituents R^2.

4.- A compound according to claim 3 wherein A represents imidazole, pyrazole, isoxazole or oxazole which can be optionally substituted with one or two substituents R^2.

5.- A compound according to claim 4 wherein A represents imidazole which can be optionally substituted with one substituent R^2.

6.- A compound according to any of claims 1 to 5 wherein each R^2 independently represents halogen, C_{1-4} alkyl or C_{1-4} haloalkyl, or two substituents R^2 on the same carbon atom can be taken together to form an oxo group.

7.- A compound according to any of claims 1 to 6 wherein D represents either phenyl optionally substituted with a fluoro atom or D is pyridine.

8.- A compound according to claim 7 wherein D represents phenyl optionally substituted with a fluoro atom.

9.- A compound according to claim 8 wherein D represents phenyl.

10.- A compound according to any of claims 1 to 9 wherein L represents a single bond or -O-.

11.- A compound according to claim 10 wherein L represents a single bond.

12.- A compound according to any of claims 1 to 11 wherein B represents phenyl, heteroaryl or C_{3-7} cycloalkyl, which can all be optionally substituted with one to three substituents R^4.

13.- A compound according to claim 12 wherein B represents phenyl optionally substituted with one to three groups R^4 or B represents cyclohexyl.

14.- A compound according to claim 13 wherein B represents phenyl optionally substituted with one to three groups R^4.

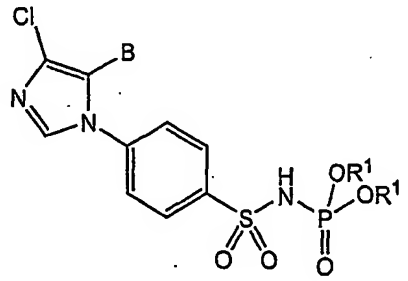
15.- A compound according to claim 10 wherein L represents -O-.

16.- A compound according to claim 15 wherein B represents C_{1-6} alkyl or phenyl optionally substituted with one to three substituents R^4.

17.- A compound according to claim 16 wherein B represents isopropyl or phenyl optionally substituted with one to three substituents R^4.

18.- A compound according to any of claims 1 to 17 wherein each R^4 independently represents halogen, C_{1-4} alkyl, C_{1-4} alkoxy or C_{1-4} haloalkyl.

19.- A compound according to claim 1 of formula **Id**:



Id

wherein:

B represents phenyl optionally substituted with one to three groups R^4; and

each R^4 independently represents halogen, C_{1-4} alkyl, C_{1-4} alkoxy or C_{1-4}

haloalkyl.

20.- A compound according to claim 19 wherein B represents 3-fluoro-4-methoxyphenyl.

21.- A compound according to any of claims 1 to 20 wherein each R^1 independently represents hydrogen, C_{1-6} alkyl or phenyl optionally substituted with one or more halogen, C_{1-4} alkyl or C_{1-4} alkoxy groups.

22.- A compound according to claim 1 selected from:

diethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;

N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic acid;

trisodium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;

tripotassium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;

dipotassium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;

calcium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;

tricalcium di-[N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate];

diethyl N-[4-[4-chloro-5-(4-ethoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;

N-[4-[4-chloro-5-(4-ethoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic acid;

diphenyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;

dimethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;

diethyl N-[4-[5-(*p*-tolyl)-3-(trifluoromethyl)pyrazol-1-yl]phenylsulfonyl]phosphoramidate;

N-[4-[5-(*p*-tolyl)-3-(trifluoromethyl)pyrazol-1-yl]phenylsulfonyl]phosphoramidic acid;

diethyl N-[4-(5-methyl-3-phenylisoxazol-4-yl)phenylsulfonyl]phosphoramidate;

N-[4-(5-methyl-3-phenylisoxazol-4-yl)phenylsulfonyl]phosphoramidic acid;
diethyl N-[4-[4-cyclohexyl-2-methyloxazol-5-yl]-2-fluorophenylsulfonyl]phosphoramidate; and
N-[4-[4-cyclohexyl-2-methyloxazol-5-yl]-2-fluorophenylsulfonyl]phosphoramidic acid;
and the salts and solvates thereof.

23.- A compound according to claim 1 selected from:
diethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
diethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate sodium salt;
diethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate potassium salt;
ethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate sodium salt;
ethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate potassium salt;
N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic acid;
trisodium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
tripotassium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
dipotassium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
calcium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
tricalcium di-[N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate];
diethyl N-[4-[4-chloro-5-(4-ethoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
N-[4-[4-chloro-5-(4-ethoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic acid;

diphenyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;

diphenyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate sodium salt;

dimethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;

dimethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate sodium salt;

dimethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate potassium salt;

methyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate sodium salt;

diethyl N-[4-[5-(*p*-tolyl)-3-(trifluoromethyl)pyrazol-1-yl]phenylsulfonyl]phosphoramidate;

N-[4-[5-(*p*-tolyl)-3-(trifluoromethyl)pyrazol-1-yl]phenylsulfonyl]phosphoramidic acid;

diethyl N-[4-(5-methyl-3-phenylisoxazol-4-yl)phenylsulfonyl]phosphoramidate;

N-[4-(5-methyl-3-phenylisoxazol-4-yl)phenylsulfonyl]phosphoramidic acid;

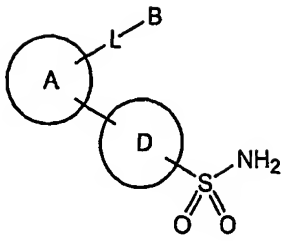
diethyl N-[4-[4-cyclohexyl-2-methyloxazol-5-yl]-2-fluorophenylsulfonyl]phosphoramidate; and

N-[4-[4-cyclohexyl-2-methyloxazol-5-yl]-2-fluorophenylsulfonyl]phosphoramidic acid.

24.- A compound according to claim 1 wherein the compound is N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic acid, and the salts and solvates thereof.

25.- Process for preparing a compound of formula I according to claim 1 which comprises:

(a) when in a compound of formula I each R^1 is different from hydrogen, reacting a sulfonamide of formula II



II

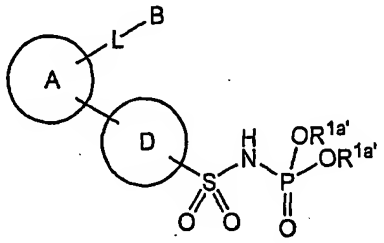
wherein A, L, B and D have the meaning described in claim 1, with a compound of formula III

$$XP(O)(OR^{1a})_2$$

III

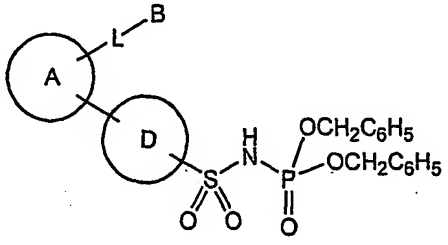
wherein X represents H or Cl and wherein each R^{1a} independently represents any of the meanings described for R^1 in claim 1 except for hydrogen, in the presence of a base, or alternatively, reacting a sulfonamide of formula II in which the group $-SO_2NH_2$ is in anionic form with a compound of formula III;

(b) when in a compound of formula I each R^1 represents hydrogen, hydrolysing a compound of formula Ia'



Ia'

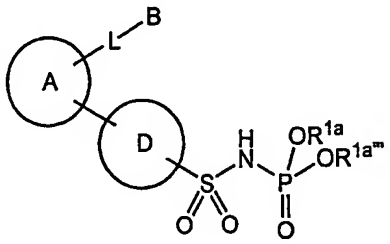
wherein A, L, B and D have the meaning described in claim 1 and wherein $R^{1a'}$ represents any of the meanings described for R^1 in claim 1 except for hydrogen and benzyl, or alternatively, hydrogenating a compound of formula Ia''



Ia''

wherein A, L, B and D have the meaning described in claim 1;

(c) when in a compound of formula I one of the substituents R^1 represents hydrogen and the other is different from hydrogen, monodealkylating a compound of formula Ia'''



Ia'''

wherein A, L, B, D and R^{1a} have the meaning described above and wherein $R^{1a'''}$ represents C_{1-6} alkyl, C_{1-6} haloalkyl or phenylC_{1-3} alkyl, where the phenyl group can be optionally substituted with one or more halogen, C_{1-4} alkyl or C_{1-4} alkoxy groups;

(d) transforming, in one or a plurality of steps, a compound of formula I into another compound of formula I; and

(e) if desired, after the above steps, reacting a compound of formula I with a base or an acid to give the corresponding addition salt.

26.- A pharmaceutical composition which comprises an effective amount of a compound of formula I according to any of claims 1 to 24 or a pharmaceutically acceptable salt or solvate thereof and one or more pharmaceutically acceptable excipients.

27.- Use of a compound of formula I according to any of claims 1 to 24 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for the treatment or prevention of diseases mediated by cyclooxygenase.

28.- Use of a compound of formula I according to any of claims 1 to 24 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for the treatment or prevention of disesases mediated by cyclooxygenase-2.

29.- Use according to claim 28 wherein the disease mediated by cyclooxygenase-2 is selected from inflammation, pain, fever, pathologies associated with prostanoid-induced smooth muscle contraction, preneoplasic disorders, cancer, cerebral infarction, epilepsy, type I diabetes, neurodegenerative diseases and

vascular diseases with an inflammatory component.

30.- Use according to claim 29 wherein the disease mediated by cyclooxygenase-2 is selected from inflammation, pain and fever.

31.- Use according to claim 29 wherein the disease mediated by cyclooxygenase-2 is a preneoplasic disorder.

32.- Use according to claim 31 wherein the preneoplasic disorder is familial adenomatous polyposis.

33.- Use according to claim 29 wherein the disease mediated by cyclooxygenase-2 is cancer.

34.- Use according to claim 33 wherein the cancer is a gastrointestinal cancer.

35.- Use according to claim 34 wherein the gastrointestinal cancer is colon cancer.

36.- Use according to claim 29 wherein the disease mediated by cyclooxygenase-2 is a neurodegenerative disease.

37.- Use according to claim 36 wherein the neurodegenerative disease is selected from dementia, Parkinson's disease and amyotrophic lateral sclerosis.

38.- Use according to claim 37 wherein the dementia is Alzheimer's disease.

39.- Use according to claim 29 wherein the disease mediated by cyclooxygenase-2 is a vascular disease with an inflammatory component.

40.- Use according to claim 39 wherein the vascular disease with an inflammatory component is atherosclerosis.

41.- Use according to claim 28 wherein the disease mediated by cyclooxygenase-2 is selected from the group consisting of: pain resulting from surgery or dental surgery; low back and neck pain; headache; toothache; pain associated with cancer; neuralgia; arthritis, including rheumatoid arthritis and juvenile arthritis; degenerative joint diseases, including osteoarthritis; gout; ankylosing spondylitis; tendinitis; pain and/or inflammation associated with traumatisms such as sprains, strains and other similar injuries, such as those produced during sport performance; synovitis; myositis; dysmenorrhea; inflammatory bowel disease; ocular inflammatory diseases, including conjunctivitis and endophthalmitis; corneal transplants; skin inflammatory diseases, including psoriasis, burns, eczema and dermatitis; systemic inflammatory processes, including sepsis and pancreatitis; bursitis; lupus erythematosus; common cold; rheumatic fever; symptoms associated with influenza or other viral infections; preterm labour;

asthma; bronchitis; familial adenomatous polyposis; cancer, including liver, bladder, pancreas, ovary, prostate, cervix, lung, breast, skin cancer and gastrointestinal cancers such as colon cancer; cerebral infarction; epilepsy; type I diabetes; dementia, including Alzheimer's disease; Parkinson's disease; amyotrophic lateral sclerosis; and atherosclerosis.